

## SEQUENCE LISTING

<120> BILIVERDIN REDUCTASE FRAGMENTS AND VARIANTS, AND METHODS OF USING BILIVERDIN REDUCTASE AND SUCH FRAGMENTS AND VARIANTS

<130> 176/60792

<140> 09/606,129

<141> 2000-06-28

<150> 60/141,309

<151> 1999-06-28

<150> 60/163,223

<151> 1999-11-03

<160> 37

<170> PatentIn Ver. 2.1

<210> 1

<211> 296

<212> PRT

<213> Homo sapiens

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Met Asn Ala Glu Pro Glu Arg Lys Phe Gly Val Val Val Val Gly Val

Gly Arg Ala Gly Ser Val Arg Met Arg Asp Leu Arg Asn Pro His Pro 20 25 30

Ser Ser Ala Phe Leu Asn Leu Ile Gly Phe Val Ser Arg Arg Glu Leu 35 40

Gly Ser Ile Asp Gly Val Gln Gln Ile Ser Leu Glu Asp Ala Leu Ser 55

Ser Gln Glu Val Glu Val Ala Tyr Ile Cys Ser Glu Ser Ser His 70 75

Glu Asp Tyr Ile Arg Gln Phe Leu Asn Ala Gly Lys His Val Leu Val

Glu Tyr Pro Met Thr Leu Ser Leu Ala Ala Ala Gln Glu Leu Trp Glu

100 105 110

Leu Ala Glu Gln Lys Gly Lys Val Leu His Glu Glu His Val Glu Leu
115 120 125

Leu Met Glu Glu Phe Ala Phe Leu Lys Lys Glu Val Val Gly Lys Asp 130 135 140

Leu Leu Lys Gly Ser Leu Leu Phe Thr Ser Asp Pro Leu Glu Glu Asp 145 150 155 160

Arg Phe Gly Phe Pro Ala Phe Ser Gly Ile Ser Arg Leu Thr Trp Leu 165 170 175

Val Ser Leu Phe Gly Glu Leu Ser Leu Val Ser Ala Thr Leu Glu Glu 180 185 190

Arg Lys Glu Asp Gln Tyr Met Lys Met Thr Val Cys Leu Glu Thr Glu 195 200 205

Lys Lys Ser Pro Leu Ser Trp Ile Glu Glu Lys Gly Pro Gly Leu Lys 210 225

Arg Asn Arg Tyr Leu Ser Phe His Phe Lys Ser Gly Ser Leu Glu Asn 225 230 235 240

Val Pro Asn Val Gly Val Asn Lys Asn Ile Phe Leu Lys Asp Gln Asn 245 250 255

Ile Phe Val Gln Lys Leu Leu Gly Gln Phe Ser Glu Lys Glu Leu Ala 260 265 270

Ala Glu Lys Lys Arg Ile Leu His Cys Leu Gly Leu Ala Glu Glu Ile 275 280 285

Gln Lys Tyr Cys Cys Ser Arg Lys 290 295

<210> 2

<211> 1070

<212> DNA

<213> Homo sapiens

<400> 2

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ggettegtgt egagaaggga getegggage attgatggag teeageagat ttetttggag 240 gatgctcttt ccagccaaga ggtggaggtc gcctatatct gcagtgagag ctccagccat 300 gaggactaca tcaggcagtt ccttaatgct ggcaagcacg tccttgtgga ataccccatg 360 acactgtcat tggcggccgc tcaggaactg tgggagctgg ctgagcagaa aggaaaagtc 420 ttgcacgagg agcatgttga actcttgatg gaggaattcg ctttcctgaa aaaagaagtg 480 gtggggaaag acctgctgaa agggtcgctc ctcttcacat ctgacccgtt ggaagaagac 540 eggtttgget teeetgeatt eageggeate tetegaetga eetggetggt eteeetettt 600 ggggagcttt ctcttgtgtc tgccactttg gaagagcgaa aggaagatca gtatatgaaa 660 atgacagtgt gtctggagac agagaagaaa agtccactgt catggattga agaaaaagga 720 cctggtctaa aacgaaacag atatttaagc ttccatttca agtctgggtc cttggagaat 780 gtgccaaatg taggagtgaa taagaacata tttctgaaag atcaaaatat atttgtccag 840 aaactettgg gecagttete tgagaaggaa etggetgetg aaaagaaacg cateetgeae 900 tgcctggggc ttgcagaaga aatccagaaa tattgctgtt caaggaagta agaggaggag 960 gtgatgtage acttecaaga tggeaceage atttggttet teteaagagt tgaceattat 1020 1070

<210> 3

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<212> PRT

<213> Homo sapiens

<400> 3

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Gly Arg Ala Gly Ser Val Arg Met Arg Asp Leu Arg Asn Pro His Pro 20 25 30

Ser Ser Ala Phe Leu Asn Leu Ile Gly Phe Val Ser Arg Arg Glu Leu
35 40 45

Gly Ser Ile Asp Gly Val Gln Gln Ile Ser Leu Glu Asp Ala Leu Ser 50 55 60

Ser Gln Glu Val Glu Val Ala Tyr Ile Cys Ser Glu Ser Ser His 65 70 75 80

Glu Asp Tyr Ile Arg Gln Phe Leu Asn Ala Gly Lys His Val Leu Val
85 90 95

Glu Tyr Pro Met Thr Leu Ser Leu Ala Ala Ala Gln Glu Leu Trp Glu 100 105 110

Leu Ala Glu Gln Lys Gly Lys Val Leu His Glu Glu His Val Glu Leu
115 120 125

Leu Met Glu Glu Phe Ala Phe Leu Lys Lys Glu Val Val Gly Lys Asp

130 135 140

Leu Leu Lys Gly Ser Leu Leu Phe Thr Ala Gly Pro Leu Glu Glu Glu 145 150 155 160

Arg Phe Gly Phe Pro Ala Phe Ser Gly Ile Ser Arg Leu Thr Trp Leu 165 170 175

Val Ser Leu Phe Gly Glu Leu Ser Leu Val Ser Ala Thr Leu Glu Glu 180 185 190

Arg Lys Glu Asp Gln Tyr Met Lys Met Thr Val Cys Leu Glu Thr Glu 195 200 205

Lys Lys Ser Pro Leu Ser Trp Ile Glu Glu Lys Gly Pro Gly Leu Lys 210 215 220

Arg Asn Arg Tyr Leu Ser Phe His Phe Lys Ser Gly Ser Leu Glu Asn 225 230 235 240

Val Pro Asn Val Gly Val Asn Lys Asn Ile Phe Leu Lys Asp Gln Asn 245 250 255

Ile Phe Val Gln Lys Leu Leu Gly Gln Phe Ser Glu Lys Glu Leu Ala 260 265 270

Ala Glu Lys Lys Arg Ile Leu His Cys Leu Gly Leu Ala Glu Glu Ile 275 280 285

Gln Lys Tyr Cys Cys Ser Arg Lys 290 295

<210> 4

<211> 295

<212> PRT

<213> Rattus norvegicus

<400> 4

Met Asp Ala Glu Pro Lys Arg Lys Phe Gly Val Val Val Val Gly Val

Gly Arg Ala Gly Ser Val Arg Leu Arg Asp Leu Lys Asp Pro Arg Ser 20 25 30

Ala Ala Phe Leu Asn Leu Ile Gly Phe Val Ser Arg Arg Glu Leu Gly 35 40 45

- Ser Leu Asp Glu Val Arg Gln İle Ser Leu Glu Asp Ala Leu Arg Ser 50 55 60
- Gln Glu Ile Asp Val Ala Tyr Ile Cys Ser Glu Ser Ser Ser His Glu 65 70 75 .80
- Asp Tyr Ile Arg Gln Phe Leu Gln Ala Gly Lys His Val Leu Val Glu 85 90 95
- Tyr Pro Met Thr Leu Ser Phe Ala Ala Ala Gln Glu Leu Trp Glu Leu 100 105 110
- Ala Ala Gln Lys Gly Arg Val Leu His Glu Glu His Val Glu Leu Leu 115 120 125
- Met Glu Glu Phe Glu Phe Leu Arg Arg Glu Val Leu Gly Lys Glu Leu 130 135 140
- Leu Lys Gly Ser Leu Arg Phe Thr Ala Ser Pro Leu Glu Glu Glu Arg 145 150 155 160
- Phe Gly Phe Pro Ala Phe Ser Gly Ile Ser Arg Leu Thr Trp Leu Val 165 170 175
- Ser Leu Phe Gly Glu Leu Ser Leu Ile Ser Ala Thr Leu Glu Glu Arg 180 185 190
- Lys Glu Asp Gln Tyr Met Lys Met Thr Val Gln Leu Glu Thr Gln Asn 195 200 205
- Lys Gly Leu Leu Ser Trp Ile Glu Glu Lys Gly Pro Gly Leu Lys Arg 210 215 220
- Asn Arg Tyr Val Asn Phe Gln Phe Thr Ser Gly Ser Leu Glu Glu Val 225 230 235 240
- Pro Ser Val Gly Val Asn Lys Asn Ile Phe Leu Lys Asp Gln Asp Ile 245 250 255
- Phe Val Gln Lys Leu Leu Asp Gln Val Ser Ala Glu Asp Leu Ala Ala 260 265 270
- Glu Lys Lys Arg Ile Met His Cys Leu Gly Leu Ala Ser Asp Ile Gln 275 280 285
- Lys Leu Cys His Gln Lys Lys 290 295

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gaaatttgga gtggtagtgg ttggtgttgg cagagctggc tcggtgaggc tgagggactt 180
gaaggatcca cgctctgcag cattcctgaa cctgattgga tttgtgtcca gacgagagct 240
tgggagcctt gatgaagtac ggcagatttc tttggaagat gctctccgaa gccaagagat 300
tgatgtcgcc tatatttgca gtgagagttc cagccatgaa gactatatac ggcagtttct 360
gcaggetgge aagcatgtee tegtggaata ecceatgaca etgteatttg eggeggeeca 420
ggagetgtgg gagetggeeg cacagaaagg gagagteetg catgaggage acgtggaact 480
cttgatggag gaattcgaat tcctgagaag agaagtgttg gggaaagagc tactgaaagg 540
gtctcttcgc ttcacagcta gcccactgga agaagagaga tttggcttcc ctgcgttcag 600
eggeatttet egeetgaeet ggetggtete eetetteggg gagetttete ttatttetge 660
caccttggaa gagcgaaaag aggatcagta tatgaaaatg accgtgcagc tggagaccca 720
gaacaagggt ctgctgtcat ggattgaaga gaaagggcct ggcttaaaaa gaaacagata 780
tgtaaacttc cagttcactt ctgggtccct ggaggaagtg ccaagtgtag gggtcaataa 840
gaacattttc ctgaaagatc aggatatatt tgttcagaag ctcttagacc aggtctctgc 900
agaggacctg gctgctgaga agaagcgcat catgcattgc ctggggctgg ccagcgacat 960
ccagaagctt tgccaccaga agaagtgaag aggaagcttc agagacttct gaagggggcc 1020
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                                                                  1081
<210> 6
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<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: hydrophobic
      domain of BVR
<220>
<221> PEPTIDE
<222> (2)
<223> where X is any aa
<400> 6
Phe Xaa Val Val Val
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<210> 7

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<211> 6
 <212> PRT
 <213> Artificial Sequence
 <223> Description of Artificial Sequence: nucleotide
       binding domain of BVR
 <220>
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 <222> (2)
 <223> where X is any aa
 <220>
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 <222> (4)..(5)
 <223> where X is any aa
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 <210> 8
 <211> 8
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> Description of Artificial Sequence:
       oxidoreductase domain of BVR
 <400> 8
 Ala Gly Leu His Val Leu Val Glu
                   5
   1
 <210> 9
 <211> 29
 <212> PRT
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       zipper of BVR
 <220>
 <221> PEPTIDE
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7

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<222> (2)..(7)
<223> where X is any aa
<220>
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<222> (9)..(14)
<223> where X is any aa
<220>
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Leu Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa Xaa Xaa Xaa Xaa Lys Xaa
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                                                         15
Xaa Xaa Xaa Xaa Leu Xaa Xaa Xaa Xaa Xaa Leu
             20
                                 25
<210> 10
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<212> PRT
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<223> Description of Artificial Sequence: kinase motif
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<400> 10
Ser Arg Arg
  1
<210> 11
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<223> Description of Artificial Sequence: kinase motif
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Lys Gly Ser
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Phe Thr Xaa
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<211> 7
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<223> Description of Artificial Sequence: nuclear
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Gly Leu Lys Arg Asn Arg Tyr
<210> 14
<211> 5
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<223> Description of Artificial Sequence: methylation
      site of BVR
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Pro Gly Leu Lys Arg
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<222> (3)..(12)
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His Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Cys
                 5
                                     10
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<211> 7
<212> PRT
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     kinase C enhancing domain
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<221> PEPTIDE
<222> (5)
<223> where X is any aa
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Lys Lys Arg Ile Xaa His Cys
<210> 17
<211> 8
<212> PRT
<213> Artificial Sequence
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<220>
<223> Description of Artificial Sequence: protein
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<220>
<221> PEPTIDE
<222> (3)
<223> where X is any aa
<220>
<221> PEPTIDE
<222> (5)..(7)
<223> where X is any aa
<400> 17
Gln Lys Xaa Cys Xaa Xaa Xaa Lys
<210> 18
<211> 7
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: protein
      kinase C enhancer peptide of rBVR
<400> 18
Lys Lys Arg Ile Met His Cys
<210> 19
<211> 8
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence: protein
      kinase C inhibitor peptide of rBVR
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Gln Lys Leu Cys His Gln Lys Lys
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<210> 20
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<211> 1014

<212> PRT

<213> Homo sapiens

<400> 20

Met Ala Glu Ser Ser Asp Lys Leu Tyr Arg Val Glu Tyr Ala Lys Ser 1 5 10 15

Gly Arg Ala Ser Cys Lys Lys Cys Ser Glu Ser Ile Pro Lys Asp Ser 20 25 30

Leu Arg Met Ala Ile Met Val Gln Ser Pro Met Phe Asp Gly Lys Val
35 40 45

Pro His Trp Tyr His Phe Ser Cys Phe Trp Lys Val Gly His Ser Ile 50 55 60

Arg His Pro Asp Val Glu Val Asp Gly Phe Ser Glu Leu Arg Trp Asp 65 70 75 80

Asp Gln Gln Lys Val Lys Lys Thr Ala Glu Ala Gly Gly Val Thr Gly 85 90 95

Lys Gly Gln Asp Gly Ile Gly Ser Lys Ala Glu Lys Thr Leu Gly Asp 100 105 110

Phe Ala Ala Glu Tyr Ala Lys Ser Asn Arg Ser Thr Cys Lys Gly Cys 115 120 125

Met Glu Lys Ile Glu Lys Gly Gln Val Arg Leu Ser Lys Lys Met Val 130 135 140

Asp Pro Glu Lys Pro Gln Leu Gly Met Ile Asp Arg Trp Tyr His Pro 145 150 155 160

Gly Cys Phe Val Lys Asn Arg Glu Glu Leu Gly Phe Arg Pro Glu Tyr 165 170 175

Ser Ala Ser Gln Leu Lys Gly Phe Ser Leu Leu Ala Thr Glu Asp Lys 180 185 190

Glu Ala Leu Lys Lys Gln Leu Pro Gly Val Lys Ser Glu Gly Lys Arg 195 200 205

Lys Gly Asp Glu Val Asp Gly Val Asp Glu Val Ala Lys Lys Ser 210 215 220

Lys Lys Glu Lys Asp Lys Asp Ser Lys Leu Glu Lys Ala Leu Lys Ala

225					230					235					240
Gln	Asn	Asp	Leu	Ile 245	Trp	Asn	Ile	Lys	Asp 250	Glu	Leu	Lys	Lys	Val 255	Cys
Ser	Thr	Asn	Asp 260	Leu	Lys	Glu	Leu	Leu 265	Ile	Phe	Asn	Lys	Gln 270	Gln	Val
Pro	Ser	Gly 275	Glu	Ser	Ala	Ile	Leu 280	Asp	Arg	Val	Ala	Asp 285	Gly	Met	Val
Phe	Gly 290	Ala	Leu	Leu	Pro	Cys 295	Glu	Glu	Суѕ	Ser	Gly 300	Gln	Leu	Val	Phe
Lys 305	Ser	Asp	Ala	Tyr	Tyr 310	Cys	Thr	Gly	Asp	Val 315	Thr	Ala	Trp	Thr	Lys 320
Cys	Met	Val	Lys	Thr 325	Gln	Thr	Pro	Asn	Arg 330	Lys	Glu	Trp	Val	Thr 335	Pro
Lys	Glu	Phe	Arg 340	Glu	Ile	Ser	Tyr	Leu 345	Lys	Lys	Leu	Lys	Val 350	Lys	Lys
Gln	Asp	Arg 355	Ile	Phe	Pro	Pro	Glu 360	Thr	Ser	Ala	Ser	Val 365	Ala	Ala	Thr
Pro	Pro 370	Pro	Ser	Thr	Ala	Ser 375	Ala	Pro	Ala	Ala	Val 380	Asn	Ser	Ser	Ala
Ser 385	Ala	Asp	Lys	Pro	Leu 390	Ser	Asn	Met	Lys	Ile 395	Leu	Thr	Leu	Gly	Lys 400
Leu	Ser	Arg	Asn	Lys 405	Asp	Glu	Val	Lys	Ala 410	Met	Ile	Glu	Lys	Leu 415	Gly
Gly	Lys	Leu	Thr 420	Gly	Thr	Ala	Asn	Lys 425	Ala	Ser	Leu	Cys	Ile 430	Ser	Thr
Lys	Lys	Glu 435	Val	Glu	Lys	Met	Asn 440	Lys	Lys	Met	Glu	Glu 445	Val	Lys	Glu
Ala	Asn 450	Ile	Arg	Val	Val	Ser 455	Glu	Asp	Phe	Leu	Gln 460	Asp	Val	Ser	Ala
Ser 465	Thr	Lys	Ser	Leu	Gln 470	Glu	Leu	Phe	Leu	Ala 475	His	Ile	Leu	Ser	Pro 480
	_	_		_		_	_		_	_	_	_	_		

Trp Gly Ala Glu Val Lys Ala Glu Pro Val Glu Val Val Ala Pro Arg

				485					490					495	
Gly	Lys	Ser	Gly 500	Ala	Ala	Leu	Ser	Lys 505	Lys	Ser	Lys	Gly	Gln 510	Val	Lys
Glu	Glu	Gly 515	Ile	Asn	Lys	Ser	Glu 520	Lys	Arg	Met	Lys	Leu 525	Thr	Leu	Lys
Gly	Gly 530	Ala	Ala	Val	qaA	Pro 535	Asp	Ser	Gly	Leu	Glu 540	His	Ser	Ala	His
Val 545	Leu	Glu	Lys	Gly	Gly 550	Lys	Val	Phe	Ser	Ala 555	Thr	Leu	Gly	Leu	Val 560
Asp	Ile	Val	Lys	Gly 565	Thr	Asn	Ser	Tyr	<b>Tyr</b> 570	Lys	Leu	Gln	Leu	Leu 575	Glu
Asp	Asp	Lys	Glu 580	Asn	Arg	Tyr	Trp	Ile 585	Phe	Arg	Ser	Trp	Gly 590	Arg	Val
Gly	Thr	Val 595	Ile	Gly	Ser	Asn	Lys 600	Leu	Glu	Gln	Met	Pro 605	Ser	Lys	Glu
Asp	Ala 610	Ile	Glu	His	Phe	Met 615	Lys	Leu	Tyr	Glu	Glu 620	Lys	Thr	Gly	Asn
Ala 625	Trp	His	Ser	Lys	Asn 630	Phe	Thr	Lys	Tyr	Pro 635	Lys	Lys	Phe	Tyr	Pro 640
Leu	Glu	Ile	Asp	Tyr 645	Gly	Gln	Asp	Glu	Glu 650	Ala	Val	Lys	Lys	Leu 655	Thr
Val	Asn	Pro	Gly 660	Thr	Lys	Ser	Lys	Leu 665	Pro	Lys	Pro	Val	Gln 670	Asp	Leu
Ile	Lys	<b>M</b> et 675	Ile	Phe	Asp	Val	Glu 680	Ser	Met	Lys	Lys	Ala 685	Met	Val	Glu
Tyr	Glu 690	Ile	Asp	Leu	Gln	Lys 695	Met	Pro	Leu	Gly	<b>Lys</b> 700	Leu	Ser	Lys	Arg
Gln 705	Ile	Gln	Ala	Ala	Tyr 710	Ser	Ile	Leu	Ser	Glu 715	Val	Gln	Gln	Ala	Val 720

Ser Gln Gly Ser Ser Asp Ser Gln Ile Leu Asp Leu Ser Asn Arg Phe

Tyr Thr Leu Ile Pro His Asp Phe Gly Met Lys Lys Pro Pro Leu Leu

730

			,					,					, , ,		
Asn	Asn	<b>Ala</b> 755	Asp	Ser	Val	Gln	Ala 760	Lys	Val	Glu	Met	Leu 765	Asp	Asn	Leu
Leu	Asp 770	Ile	Glu	Val	Ala	Tyr 775	Ser	Leu	Leu	Arg	Gly 780	Gly	Ser	Asp	Asp
Ser 785	Ser	Lys	Asp	Pro	<b>Ile</b> 790	Asp	Val	Asn	Tyr	Glu 795	Lys	Leu	Lys	Thr	Asp 800
Ile	Lys	Val	Val	Asp 805	Arg	Asp	Ser	Glu	Glu 810	Ala	Glu	Ile	Ile	Arg 815	Lys
Tyr	Val	Lys	Asn 820	Thr	His	Ala	Thr	Thr 825	His	Asn	Ala	Tyr	Asp 830	Leu	Glu
Val	Ile	Asp 835	Ile	Phe	Lys	Ile	Glu 840	Arg	Glu	Gly	Glu	Сув 845	Gln	Arg	Tyr
Lys	Pro 850	Phe	Lys	Gln	Leu	His 855	Asn	Arg	Arg	Leu	Leu 860	Trp	His	Gly	Ser
Arg 865	Thr	Thr	Asn	Phe	Ala 870	Gly	Ile	Leu	Ser	Gln 875	Gly	Leu	Arg	Ile	Ala 880
Pro	Pro	Glu	Ala	Pro 885	Val	Thr	Gly	Tyr	Met 890	Phe	Gly	Lys	Gly	Ile 895	Tyr
Phe	Ala	Asp	Met 900	Val	Ser	Lys	Ser	Ala 905	Asn	Tyr	Cys	His	Thr 910	Ser	Gln
Gly	Asp	Pro 915	Ile	Gly	Leu	Ile	Leu 920	Leu	Gly	Glu	Val	Ala 925	Leu	Gly	Asn
Met	Tyr 930	Glu	Leu	Lys	His	Ala 935	Ser	His	Ile	Ser	Lys 940	Leu	Pro	Lys	Gly
Lys 945	His	Ser	Val	Lys	Gly 950	Leu	Gly	Lys	Thr	Thr 955	Pro	Asp	Pro	Ser	<b>Ala</b> 960
Asn	Ile	Ser	Leu	Asp 965	Gly	Val	Asp	Val	Pro 970	Leu	Gly	Thr	Gly	Ile 975	Ser
Ser	Gly	Val	Asn 980	Asp	Thr	Ser	Leu	Leu 985	Tyr	Asn	Glu	Tyr	Ile 990	Val	Tyr

Asp Ile Ala Gln Val Asn Leu Lys Tyr Leu Leu Lys Leu Lys Phe Asn

995 1000 1005

Phe Lys Thr Ser Leu Trp 1010

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<223> Description of Artificial Sequence: probe
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